REMARKS

Claims 1, 7, 9 and 10 were pending in the subject application. By the amendment, Claims 7 and 9 have been canceled without prejudice or disclaimer, Claims 1 and 10 have been amended, and new Claims 64-67 have been added. Applicant maintains that the claim amendments do not raise an issue of new matter. Support for the amendments to Claim 1 can be found at least in previous Claim 9, in paragraph [0023] on page 6 of the application as filed, and in the previous version of the claim. Support for the amendments to Claim 10 can be found at least the previous version of the claim. Support for new Claims 64 and 65 can be found at least in Claims 1 and 10, respectively. Support for new Claims 66 and 67 can be found at least in paragraph [0074] on pages 16-17 of the application as filed. Entry of the amendments is respectfully requested.

Provisional Obviousness-type Double Patenting Rejections

1. Claims 1 and 9 are provisionally rejected as being unpatentable over Claims 1-4 and 42 of co-pending U.S. Patent Application 10/984,683 in view of Sanchez (US2002/0086899).

Applicant notes that Claims 1-4 and 42 of U.S. Patent Application 10/984,683 have been canceled. New pending claims 99-128 were filed in US 10/984,683 in an amendment dated June 20, 2008. Claims 99 and 114 are independent claims.

Claims 99 and 114 recite:

> 99. A method for treating a mood disorder in a patient comprising administering to the patient pipamperon and a selective serotonin and nor-adrenaline re-uptake inhibitor (SNRI) to treat the mood disorder in the patient, wherein pipamperon is administered in a dose ranging between 5 and 15 mg and wherein pipamperon is administered simultaneously with, separate from or sequential to administration of the SNRI.
>
> 114. A method for treating a mood disorder in a patient comprising administering to the patient a pharmaceutical composition comprising

pipamperon and a selective serotonin and nor-adrenaline re-uptake inhibitor (SNRI) to treat the mood disorder in the patient.

Thus, the claims in US 10/984,683 recite treating a "mood disorder" whereas the present claims are directed to treating an "anxiety disorder", and the claims in US 10/984,683 recite administering a "selective serotonin and nor-adrenaline re-uptake inhibitor (SNRI)" whereas the present claims recite administering "a selective serotonin re-uptake inhibitor (SSRI)."

2. Applicant acknowledges the provisional rejection of Claims 1, 9 and 10 over Claims 82-84 and 100-101 of later-filed co-pending U.S. Patent Application 10/580,962.

Rejections under 35 U.S.C. §112 First Paragraph

Claims 1, 7, 9 and 10 are rejected as failing to comply with the written description and enablement requirements of 35 U.S.C. §112, first paragraph.

Claim 1 has herein above been amended to specify that pipamperone and the selective serotonin re-uptake inhibitor (SSRI) are simultaneously administered to the patient, to specify that the indicated dose of pipamperone is a daily dose, and to limit the claim to specific SSRIs.

Applicant would also like to direct the Examiner's attention to applicant's Experimental Examples presented in related U.S. Patent Application Nos. 10/984,683 [US 2005/0203130] and 10/580,962 [US 2007/0078162]. The Examples show the advantages of using pipamperone with citalopram to treat depression (Example 3), obsessive-compulsive disorder (Example 4), and panic disorder (Example 5). Obsessive-compulsive disorder and panic disorder are types of anxiety disorders (see, for example, "Diagnostic and Statistical Manual of Mental Disorders" published by the American

Psychiatric Association, which is referred to in paragraph [0058] on page 13 of the present application).

In the present application, the inventor provides an explanation for the advantage of this combined treatment, as set forth in paragraphs [0042]-[0045] on pages 10-11:

> "The inventor has found that the non-response to selective serotonin re-uptake inhibitors (SSRIs) in depression may be declared by (partial) inhibition of the 5-HT1A stimulation via 5-HT2A stimulation. Des-inhibition thereof via 5-HT2A antagonism seems to be an answer to this problem.
>
> The present inventor has found that a simultaneous or foregoing treatment with a compound having a high selective 5-HT2A antagonist, inverse agonist or partial agonist activity, could lead to a greater response towards SSRIs. However, not all compounds exhibiting 5-HT2A antagonism are useful: competition between 5-HT2A stimulation via serotonin and 5-HT2A antagonism via the compound could be responsible for the lack of more efficacy of compounds which have both a selective serotonin re-uptake inhibitory and 5-HT2A antagonist profile, such as trazodone and nefazodone.
>
> The present inventor has further surprisingly found that a simultaneous or foregoing treatment with a compound having a high selective D4 antagonist, inverse agonist or partial agonist activity in combination with a compound having a high selective 5-HT2A antagonist, inverse agonist or partial agonist activity could lead to a greater response towards SSRIs.
>
> The present inventor has found that a compound which binds to the 5-HT2A receptor with a pKi of at least 8 but for which the binding affinity, ie pKi, towards other 5HT receptors is less than 8 in combination with a compound which has a high selective affinity for the D4 receptor, i.e. which bind to the D4 receptor with a pKi of at least 8 but for which the binding affinity, ie pKi, towards other dopamine receptors is less than 8 also show such an improved effect in treatment. These effects, ie D4 antagonism, inverse agonism or partial agonism and 5-HT2A antagonism, inverse agonism or partial agonism, preferably reside in the same compound."

Re-consideration and withdrawal of these rejections are respectfully requested in

view of the amendments and remarks made herein above.

Rejections under 35 U.S.C. §103(a)

Claims 1, 7, 9 and 10 are rejected as being unpatentable over Dipiperon (manufacture sheet) in view of Sanchez (US2002/0086899).

Applicant respectfully traverses this rejection.

Dipiperon teaches use of pipamperone, and Sanchez teaches use of escitalopram (the S-(+)-enantiomer of citalopram). Sanchez teaches that citalopram is a well known antidepressant drug (see paragraphs [0001]-[0003]).

Dipiperon teaches away from the use of pipamperone with a drug such as citalopram. Specifically, on page 3, lines 9-11, Dipiperon teaches:

> "The simultaneous use of other antipsychotics, ... antidepressants ...increases the risk of the occurrence of tardive dyskinesia."

Sanchez teaches in paragraph [0007] that escitalopram "has now been found to show potent effects in models of neurotic disorders such as anxiolytic effect and prominent effect in the treatment of panic attacks and obsessive compulsive disorder." There is no explicit teaching or motivation in Sanchez to combine escitalopram with another drug. Rather, since escitalopram is described as being "potent" for treatment, the skilled artisan would have no motivation to combine another drug with escitalopram.

Thus, neither of the cited references provides a motivation for combining administration of pipamperone with a drug such as citalopram. In contrast, Dipiperon teaches away from the use of the claimed combination.

In addition, the claimed invention requires the administration of pipamperone in a daily dose ranging between 5 and 15 mg. Dipiperon teaches away from this dose range. For adults, Dipiperon on page 1 teaches an initial dose of 40 to 80 mg a day, and that if necessary the dose may be increased to a maximum of 360 mg per day. For children the

initial dose is 20 mg per day, and the optimal therapeutic dose varies from 20 to 40 mg per day. There is no teaching or suggestion in the cited references to administer pipamperone at a lower dose than the recommended dose. Applicant respectfully maintains that the present invention does not involve a mere optimization of dosage by routine experimentation as suggested by the Examiner. Rather, as applicant pointed out in the previous reply dated February 4, 2008 "it is well-known that pipamperone at the ubiquitously used (high) prior art doses indeed decreases the symptom of psychological anxiety (see e.g. information by manufacturer attached hereto). This effect of pipamperone results from a neuroleptic-sedative effect. Specifically, it is known that the high dose pipamperone results in D2 receptor-related dopaminergic and H1 receptor-related histaminergic antagonism, which is responsible for the neuroleptic-sedative effect. This antagonizing effect (resulting in this neuroleptic-sedative effect) is absent at the claimed low dose of 5-15 mg/day. Accordingly, there would be no incentive to decrease the amount of pipamperone administered, since this would lower the neuroleptic-sedative effect."

Reconsideration and withdrawal of this rejection is respectfully requested.

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement (SIDS) is being filed to supplement the Information Disclosure Statements filed on February 11, 2008, August 23, 2007, April 11, 2007 and August 9, 2005 in connection with the subject application.

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicant would like to direct the Examiner's attention to the references that are listed on the attached forms PTO/SB/08A-B. A copy of each non-U.S. patent documents is also attached.

Status of Related European Application

Applicant would like to direct the Examiner's attention to related European Patent Application No. 04025035.9. Enclosed is a copy of a Communication dated October 13, 2008 indicating that Examining Division of the European Patent Office intends to grant a European patent on the application. The application was allowed with broad claims including uses of pipamperone and a SSRI for treating a mood disorder or anxiety disorder.

Status of U.S. Patent Family Members

Applicant would also like to advise the Examiner of the status of co-pending patent family members.

1. U.S. Patent Application No. 10/725,965. The claims have been subject to a restriction requirement. Office Actions on the merits of the application issued on January 23, 2008 and September 15, 2008.

2. U.S. Patent Application No. 10/803,793. The claims have been subject to a restriction requirement. Office Actions on the merits of the application issued on May 3, 2007, October 19, 2007 and September 2, 2008.

3. U.S. Patent Application No. 10/984,683. The claims have been subject to a restriction requirement. Office Actions on the merits of the application issued on August 10, 2007, February 22, 2008, and October 21, 2008.

4. U.S. Patent Application No. 10/580,962. An examination report has not yet issued in connection with this application.

CONCLUSIONS

In view of the amendments and remarks made herein, reconsideration and withdrawal of the rejections set forth in the May 13, 2008 Office Action are respectfully requested. If there are any minor matters preventing the allowance of the subject application, the Examiner is requested to telephone the undersigned attorney.

A check for $735.00 is enclosed for the $555.00 fee for a three month extension of time for a small entity and the $180.00 fee for submitting an Information Disclosure Statement. No additional fee is deemed necessary in connection with the submission of this reply. However, if any other fee is required with this reply or to maintain the pendency of the subject application, authorization is hereby given to withdraw the amount of any such fee from Deposit Account No. 01-1785. Overpayments may also be credited to Deposit Account No. 01-1785.

Respectfully submitted,

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Dated: November 12, 2008
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By _____
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